IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Andrew Dames et al.

Serial No. 09/787,195

Filed: September 17, 1999

For: Bio-Assay Technique

Examiner: Lyle A. Alexander

Group Art Unit: 1743

SECOND SUPPLEMENTAL DECLARATION

I, Peter Swarbrick, hereby declare that:

1. I am the same Peter Swarbrick who signed declarations dated 22 December 2005 and 21 June 2006 in respect of US patent application no. 09/787,195 entitled "Bio-Assay Technique, (hereinafter the '195 application).

2. As discussed in my 22 December 2005 and 21 June 2006 declarations, by using particles that are sized according to the dimension requirement of the claimed support, many more parallel assay tests can be simultaneously performed than would be the case with particles of the size described for example in US 5129974 (hereinafter Aurenius). In particular, paragraph 7 of my 21 June 2006 declaration explains that when barcoded particles with dimensions of 0.1 x 0.01 x 0.001 mm (i.e. particles embodying the claimed support) are contained in a standard 7 mm diameter cylindrical well (i.e. a well of an industry-standard 96-well microtitre plate), about 600 to 800 of the particles can be sufficiently isolated from each other to be readable through a transparent base of the well. Assuming that a minimum of five particles of a particular barcoded type need to be readable for statistical significance and data generation purposes, this translates into the capability to perform simultaneously between about 120 and 160 parallel assay tests.

3. By a support being "readable" I mean that (i) the spatially varying pattern which the support incorporates can be recognised, (ii) the response to the assay of probe molecules bound to the support can be recognised, and (iii) the response can be associated with the spatially varying pattern. For example, when the spatially varying pattern of a support is a barcode and when a fluorescent marker attaching to the support is used to indicate the response of the probe molecules, the support is "read" by decoding the barcode, identifying any marker attaching to the support, and associating the marker (if identified) with the decoded barcode. More

particularly, to read a support through the transparent base of a 7 mm diameter cylindrical well, the support has to appear isolated, i.e. be completely non-overlapping with other supports, so that the barcode of the support is not masked and any fluorescent signal from the support can be unambiguously associated with that barcode.

4. Now, in general, if only a few supports of a given size are present in a well, the proportion of supports that appear isolated when viewed through the base of the well increases, but on the other hand only a small number of supports are available to be read in the first place. Conversely, if many supports are present in the well, the proportion of supports that appear isolated decreases as the likelihood of support overlap goes up, but a greater number of supports are available to be read. Between these extremes, an optimum number of supports of a given size exists which maximises the number of readable supports in the well. Of course, that maximum number of readable supports will generally be less than the optimum number of supports which produces the maximum.

5. In respect of the 0.1 x 0.01 x 0.001 mm particles discussed in paragraph 2 above, the range of about 600 to 800 readable particles results from having about the optimum number of particles of that size in the 7 mm diameter cylindrical well.

6. In contrast, and with reference to paragraph 5 of my 21 June 2006 declaration, when larger plate-like particles with dimensions of 0.3 x 0.6 mm (i.e. greater dimensions than the claimed support) are contained in and viewed through the transparent base of a 7 mm diameter cylindrical well, I find that only about 12 to 15 particles are sufficiently isolated to be readable when about the optimum number of particles of that size is in the well.

7. The following table provides values (for differently sized particles) of the number of particles that I would expect to be able to read through the transparent base of a 7 mm diameter cylindrical well when about the optimum number of particles is in the well for the respective particle size. All the particles are substantially planar (i.e. have relatively small third dimensions), the value of the third dimension being omitted from the first column of the table. The 0.1 x 0.0045 mm, 0.1 x 0.01 mm and 0.1 x 0.1 mm particles embody the claimed support, whereas the 0.3 x 0.6 mm and 1.0 x 1.0 mm particles do not embody the claimed support.

Particle Size (mm)	Maximum number readable
0.1 x 0.0045	1500-2000
0.1 x 0.01	600-800
0.1 x 0.1	100-130
0.3 x 0.6	12-15
1.0 x 1.0	5-8

8. What is clear from the above table is that even the largest particle embodying the claimed support allows over an order of magnitude more particles to be read through the transparent base of a 7 mm diameter cylindrical well than would be the case with particles of the size described in Aurenius. This increase in the maximum number of readable particles translates directly into the capability to perform simultaneously more parallel assay tests.

9. I further declare that all statements made herein of my knowledge are true, and that all statements made on information and belief, including those that can be supported by citations to published scientific literature, are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the '195 application or any patent issued thereon.

17-October 2006
DATE

PETER SWARBRICK, Ph.D.